



Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.  
600-1-087CIP2I

Serial No.  
08/485,943

## INFORMATION DISCLOSURE STATEMENT

*(Use several sheets if necessary)*

Applicant  
Jeffrey Friedman et al

Filing Date  
June 7, 1995

Group  
1636

### U.S. PATENT DOCUMENTS

*Examiner Initials		Document Number	Issue Date	Name	Class	Subclass	Filing Date If Appropriate
<i>JW</i>	A25	5,073,627	12/17/91	Curtis <i>et al.</i>	530	351	
	A26	5,116,964	05/26/92	Capon <i>et al.</i>	536	27	
	A27	5,225,538	07/06/93	Capon <i>et al.</i>	536	387.3	
	A28	5,359,034	10/25/94	Skelly <i>et al.</i>	536	351	
	A29	5,428,130	06/27/95	Capon <i>et al.</i>	530	350	
	A30	5,447,851	09/05/95	Beutler <i>et al.</i>	435	69.7	
	A31	5,455,165	10/03/95	Capon <i>et al.</i>	435	64.7	
	A32	5,480,981	01/02/96	Goodwin <i>et al.</i>	536	23.5	
	A33	5,514,582	05/07/96	Capon <i>et al.</i>	435	252.3	
	A34	5,574,018	11/12/96	Habberfield <i>et al.</i>	514	21	
	A35	5,670,625	09/23/97	Lyman <i>et al.</i>	530	387.3	
	A36	5,714,147	02/03/98	Capon <i>et al.</i>	424	178.1	
	A37	5,719,266	02/17/98	DiMarchi <i>et al.</i>	530	350	
	A38	5,739,277	4/14/98	Presta <i>et al.</i>	530	326	
	A39	5,756,461	05/26/98	Stephens, T.W.	514	12	
<i>WJF</i>	A40	5,827,734	10/27/98	Weigle <i>et al.</i>	435	325	
<i>WJ</i>	A41	5,512,457	4/30/96	Lyman et al.	435	69.5	
<i>WJ</i>	A42	5,098,833	3/24/92	Lasky <i>et al.</i>	435	69.1	

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FOREIGN PATENT DOCUMENTS								
*Examiner Initials		Document Number	Publication Date	Country	Class	Subclass	Translation	
							Yes	No
JK	B78	AU-B-51978/96	03/05/98	AU			✓	
	B79	EP 0 401 384	12/12/90	EP				
	B80	WO 83/04053	11/24/83	WIPO				
	B81	WO 89/10932	11/16/89	WIPO				
	B82	WO 94/20069	09/15/94	WIPO				
	B83	WO 95/21629	08/17/95	WIPO				
	B84	WO 96/03141	02/08/96	WIPO				
	B85	WO 96/04388	02/15/96	WIPO				
	B86	WO 96/05309	02/22/96	WIPO				
	B87	WO 96/11953	04/25/96	WIPO				
	B88	WO 96/18412	06/20/96	WIPO				
	B89	WO 96/29989	10/03/96	WIPO				
JK	B90	WO 97/24137	07/10/97	WIPO				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)		
JK	C1	Altman, S.W. et al., "Expression and Purification of a Synthetic Human Obese Gene Product," <i>Protein Expression and Purification</i> , 6:722-726 (1995).

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)					
<i>JK</i>	C2	Angier, N., "Researchers Link Obesity In Humans To Flaw In A Gene," <i>The New York Times</i> reported on December 1, 1994.			
	C3	Barinaga, " 'Obese' Protein Slims Mice", <i>Science</i> , 269:475-476 (July, 1995).			
	C4	Baron, M.H. et al., "Antibodies against the Chemically Synthesized Genome-Linked Protein of Poliovirus React with Native Virus-Specific Proteins," <i>Cell</i> , 28:395-404 (February, 1982).			
	C5	Bennett, B.D. et al., "A role for leptin and its cognate receptor in hematopoiesis," <i>Current Biology</i> , 6(9):1170-1180 (September 1, 1996).			
	C9	Bishop, J.E., "Newfound Gene May Control Fat Storage," <i>The Wall Street Journal, Health and Science</i> , reported on December 1, 1994.			
	C7	Bishop, J.E., "Rockefeller Study Supports Theory That Body Has Fat-Maintenance System," <i>Wall Street Journal</i> , reported on March 9, 1995.			
	C9	Campfield, L.A. et al., "Strategies and Potential Molecular Targets for Obesity Treatment," <i>Science</i> , 280:1383-1387 (May, 1998).			
	C9	Capon, D.J. et al., "Designing CD4 immunoadhesins for AIDS therapy," <i>Nature</i> , 337:525-531 (February, 1989).			
	C10	Chen, H. et al., "Evidence That the Diabetes Gene Encodes the Leptin Receptor: Identification of a Mutation in the Leptin Receptor Gene in <i>db/db</i> Mice," <i>Cell</i> , 84:491-495 (February, 1996).			
	C11	Cioffi, J.A. et al., "Novel B219/OB receptor isoforms: Possible role of leptin in hematopoiesis and reproduction," <i>Nature Medicine</i> , 2(5):585-589 (May, 1996).			
	C12	Coleman, D.L. et al., "The Influence of Genetic Background on the Expression of the <i>Obese (Ob)</i> Gene in the Mouse," <i>Diabetologia</i> , 9:287-293 (1973).			
	C13	Comuzzie, A.G. et al., "The Search for Human Obesity Genes," <i>Science</i> , 280:1374-1377 (May, 1998).			
<i>JK</i>	C14	Considine, R.V. et al., "Ob Gene Expression Is Increased in Adipocytes from Obese Humans," <i>Diabetes</i> , 44:202A (May, 1995) (ABSTRACT 739).			

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)				
✓	C15	Cusin I. <i>et al.</i> , "The <i>ob</i> Gene and Insulin A Relationship Leading to Clues to the Understanding of Obesity," <i>Diabetes</i> , 44:1467-1470 (December, 1995).		
	C16	Detjen, J. (Philadelphia Inquirer), "Obesity gene find may help millions someday," The Durham Herald Co., <i>The Herald-Sun</i> (Durham, NC), pg. A1, reported on December 1, 1994.		
	C17	Dressman, G.R. <i>et al.</i> , "Antibody to hepatitis B surface antigen after a single inoculation of uncoupled synthetic HbsAg peptides," <i>Nature</i> , 295:158-160 (January, 1982).		
	C18	Ellison, J.W. <i>et al.</i> , "The nucleotide sequence of a human immunoglobulin C $\gamma$ 1 gene," <i>Nucleic Acids Research</i> , 10(13):4071-4079 (1982).		
	C19	Enerbäck, S. <i>et al.</i> , "Mice lacking mitochondrial uncoupling protein are cold-sensitive but not obese," <i>Nature</i> , 387:90-93 (May, 1997).		
	C20	Evans, D.J. <i>et al.</i> , "Relationship of Body Fat Topography to Insulin Sensitivity and Metabolic Profiles in Premenopausal Women," <i>Metabolism</i> , 33(1):68-75 (January, 1984).		
	C21	Ferré, P., "Obésité. Produit de Gène <i>ob</i> Et Contrôle De La Masse Adipeuse [Obesity, The <i>ob</i> Gene Product and Control of Adipose Mass]," <i>Diabète &amp; Métabolisme (Paris)</i> , 21:217-218 (1995).		
	C22	Fisher, C.J. <i>et al.</i> , "Treatment of Septic Shock with the Tumor Necrosis Factor Receptor:Fc Fusion Protein," <i>N. Engl. J. Med.</i> , 334:1697-1702 (1996).		
	C23	Flam, "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Science</i> , 266:1477-1478 (December, 1994).		
	C24	Ford, C.F. <i>et al.</i> , "Fusion Tails for the Recovery and Purification of Recombinant Proteins," <i>Protein Expression and Purification</i> , 2:95-107 (1991).		
✓	C25	Frederich, R. <i>et al.</i> , "Nutritional Regulation of <i>ob</i> Gene mRNA in White Adipose Tissue," <i>The Endocrine Society, Programs &amp; Abstracts</i> , 77th Meeting, June 14-17, 1995, Washington, D.C., p.173 (ABSTRACT OR25-3)		

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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)				
✓	C26	Frederich R.C. et al., "Leptin levels reflect body lipid content in mice: Evidence for diet-induced resistance to leptin action," <i>Nature Medicine</i> , 1(12):1311-1314 (December, 1995).		
✓	C27	GenBank Accession No. 603288, ob, Deposited by Zhang et al., March 30, 1995.		
✓	C28	GenBank Accession No. 623332, ob, Deposited by Zhang et al., January 13, 1995.		
✓	C29	GenBank Accession No. 726297, obesity protein, Deposited by Chehab et al., March 21, 1995.		
✓	C30	GenBank Accession No. U18812, <i>Mus musculus</i> obese precursor (ob) mRNA, complete cds., deposited by Zhang, Y. et al., March 30, 1995.		
✓	C31	GenBank Accession No. U18915, Human obese (ob) mRNA, complete cds., deposited by Zhang, Y. et al., January 13, 1995.		
✓	C32	GenBank Accession No. U22421, <i>Mus musculus</i> obesity protein (ob) gene, complete cds., Deposited by Chehab et al., March 23, 1995.		
✓	C33	Grundy and Barnett, "Metabolic and Health Complications of Obesity," <i>Disease-a-Month (DM)</i> , 36:645-696 (December, 1990)		
✓	C34	Gura, T., "Uncoupling Proteins Provide New Clue to Obesity's Causes," <i>Science</i> , 280:1369-1370 (May, 1998).		
✓	C35	Hamilton, B.S. et al., "Increased obese mRNA expression in omental fat cells from massively obese humans," <i>Nature Medicine</i> , 1(9):953-956 (September, 1995).		
✓	C36	Harvill, E.T. et al., "An IgG3-IL2 fusion protein activates complement, binds Fc $\gamma$ RI, generates LAK activity and shows enhanced binding to the high affinity IL-2R," <i>Immunotechnology</i> , 1:95-105 (1995).		
✓	C37	Hawkes, N. "Obesity of Mice and Men," Times Newspaper Limited, <i>The Times</i> , reported on December 5, 1994.		
✓	C38	He, Y. et al., "The Mouse <i>obese</i> Gene," <i>Journal of Biological Chemistry</i> , 270(48):28887-28891 (December, 1995).		

EXAMINER <i>Dugay</i>	DATE CONSIDERED 8/21/00
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gjf	C39	Helm, L. (Times Staff Writer), "Gene Found That May Lead To Obesity," <i>The Times Mirror Company, Los Angeles Times, part A, page 1, col. 3</i> (December 1, 1994).		
	C40	Henry R.R. et al., "Effects of Weight Loss on Mechanisms of Hyperglycemia in Obese Non-Insulin-Dependent Diabetes Mellitus," <i>Diabetes</i> , 35:990-998 (September, 1986).		
	C41	Highfield, R. (Science Editor), "Scientists find cause of fat mice and men Gene discovery from overweight rodents may help to produce drugs for people with a hereditary risk of obesity," <i>Telegraph Group Limited, The Daily Telegraph</i> , pg. 7 (December 1, 1994).		
	C42	Hill, J.O. et al., "Environmental Contributions to the Obesity Epidemic," <i>Science</i> , 280:1371-1374 (May, 1998).		
	C43	Hirsch, J., "Some heat but not enough light," <i>Nature</i> , 387:27-28 (May, 1997).		
	C44	Hodgson, " 'Obesity' Where Less is More," <i>Bio/Technology</i> , 13:1060-1063 (October, 1995).		
	C45	Hulsey, M.G. et al., "An Anorectic Agent From Adipose Tissue of Overfed Rats: Effects of Feeding Behavior," <i>Physiol. &amp; Behav.</i> , 52:1141-1149 (1992).		
	C46	Hummel, K.P. et al., "Diabetes, a New Mutation in the Mouse," <i>Science</i> , 153:1127-1128 (1966)		
	C47	Huse, W.D. et al., "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," <i>Science</i> , 246:1275-1281 (December, 1989).		
	C48	IBI FLAG BIOSYSTEM, "High Yield Expression, Detection, and Purification of Recombinant Proteins in <i>E. coli</i> ," <i>Integrated Sciences Pty Ltd, Sydney, Australia</i>		
	C49	IBI FLAG Epitope, A Technical Bulletin for Users of FLAG Technology, International Biotechnologies Inc., FLAG Product Development Group, IBI, A Kodak Company, New Haven, CT, Volume 1, Number 1, pp. 1-24 (September, 1992).		
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EXAMINER <i>Myra J. Sal</i>	DATE CONSIDERED 8/21/07
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)					
✓	C51	Ikeda, H. <i>et al.</i> , "Effects of Pioglitazone on Glucose and Lipid Metabolism in Normal and Insulin Resistant Animals," <i>Arzneim.-Forsch./Drug Res.</i> , 40 (1), Nr. 2:156-162 (1990).			
	C52	Isse N. <i>et al.</i> , "Structural Organization and Chromosomal Assignment of the Human obese Gene," <i>J. Biological Chemistry</i> , 270(46):27728-27733 (November, 1995).			
	C53	Iwanishi, M. <i>et al.</i> , "Effect of Pioglitazone on Insulin Receptors of Skeletal Muscles From High-Fat-Fed Rats," <i>Metabolism</i> , 42(8):1017-1021 (August, 1993).			
	C54	Jeanrenaud, B., "An hypothesis on the aetiology of obesity: dysfunction of the central nervous system as a primary cause," <i>Diabetologia</i> , 28:502-513 (1985).			
	C55	Jeanrenaud, B., "Central Nervous System and Peripheral Abnormalities: Clues to the Understanding of Obesity and NIDDM," <i>Diabetologia</i> , 37(Suppl. 2):S169-S178 (1994).			
	C56	Jeanrenaud, B. "Neuroendocrine and Metabolic Basis of Type II Diabetes as Studied in Animal Models," <i>Diabetes/Metabolism Reviews</i> , 4(6):603-614 (1988).			
	C57	Kaiser, E.T. <i>et al.</i> , "Amphiphilic Secondary Structure: Design of Peptide Hormones," <i>Science</i> , 223:249-255 (January, 1984).			
	C58	Kallen, C.B. <i>et al.</i> , "Antidiabetic thiazolidinediones inhibit leptin (ob) gene expression in 3T3-L1 adipocytes," <i>Proc. Natl. Acad. Sci.</i> , 93:5793-5796 (June, 1996).			
	C59	Kiberstis, P.A. <i>et al.</i> , "Regulation of Body Weight," <i>Science</i> , 280:1363 (May, 1998).			
	C60	Kissebah, A.H. <i>et al.</i> , "Health Risks of Obesity," <i>Medical Clinical North America</i> , 73(1):111-138 (January, 1989).			
	C61	Kissebah, A.H. <i>et al.</i> , "Regional Adiposity & Morbidity" in <i>Physiological Reviews: Body Fat Distribution &amp; Morbidity</i> , 74(4):761-811 (October, 1994).			
	C62	Kletzien, R.F. <i>et al.</i> , "Adipocyte Fatty Acid-Binding Protein: Regulation of Gene Expression <i>In Vivo</i> and <i>In Vitro</i> by an Insulin-Sensitizing Agent," <i>Molecular Pharmacology</i> , 42:558-562 (1992).			
✓	C63	Kobayashi, M. <i>et al.</i> , "Pioglitazone Increases Insulin Sensitivity by Activating Insulin Receptor Kinase," <i>Diabetes</i> , 41:476-483 (April, 1992).			

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	C67	Lerner, R.A., "Synthetic Vaccines," <i>Scientific American</i> , 248:66-74 (1983).		
	C68	Levin, N. <i>et al.</i> , "Decreased food intake does not completely account for adiposity reduction after ob protein infusion," <i>Proc. Natl. Acad. Sci.</i> , 93:1726-1730 (February, 1996).		
	C69	LindPaintner, K., "Clinical Implications of Basic Research: Finding an Obesity Gene-A Tale of Mice and Man," <i>New England Journal of Medicine</i> , 332(10):679-680 (March, 1995).		
	C70	Marx, J., "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Surg. Neurol.</i> , 43:351-352 (1995).		
	C71	Marx, J., "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Science</i> , 266:1477-1478 (December, 1994).		
	C72	Masuda, K. <i>et al.</i> , "Effects of Troglitazone (CS-045) on insulin secretion in isolated rat pancreatic islets and HIT cells: an insulinotropic mechanism distinct from glibenclamide," <i>Diabetologia</i> , 38:24-30 (1995).		
<i>jkf</i>	C73	Masuzaki et al., "Molecular Cloning of a Rat Obese (ob) Complement DNA - Augmented Gene Expression in Obese-Hyperglycemic Wistar Fatty Rats," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.175 (ABSTRACT P1-250)		

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✓	C74	Masuzaki, H. et al., "Adipose Tissue-specific Expression of the <i>Obese</i> (ob) Gene in Rats and Its Marked Augmentation in Genetically Obese-hyperglycemic Wistar Fatty Rats," <i>Proceedings of the Japan Academy Series B Physical and Biological Sciences</i> , 71(5):148-152 (1995).
	C75	McGarry, J.D., "Does leptin lighten the problem of obesity?" <i>Current Biology</i> , 5(12):1342-1344 (1995).
	C76	Mini-Symposium on Flag Technology, ASCB 1992, "Purification and Characterization of Cellular Proteins with the Flag Epitope," Colorado Convention Center, Denver, Colorado, 8 pages (November 18, 1992)
	C77	Mizuno, T. et al., "Elevated Expression of Obese (ob/ob) Gene Product in Adipose Tissue, and Impaired Induction by Insulin of Jun-B mRNA in Liver, in Genetically Obese Yellow Mice," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.174 (ABSTRACT P1-248)
	C78	Moinat, M. et al., "Modulation of <i>obese</i> gene expression in rat brown and white adipose tissues," <i>FEBS Letters</i> , 373:131-134 (1995).
	C79	Murakami, N. et al., "Amelioration of insulin resistance in genetically obese rodents by M16209, a new antidiabetic agent," <i>European Journal of Pharmacology</i> , 304:129-134 (1996).
	C80	Murakami, T. et al., "Cloning of Rat <i>Obese</i> cDNA and its Expression in Obese Rats," <i>Biochemical and Biophysical Research Communications</i> , 209(3):944-952 (April, 1995).
	C81	Nakamura, M.T. , "Another Obese Gene Function," <i>Nature</i> , 374:124 (March, 1995)
	C82	Ogawa, et al., "Region-Specificities of the Obese (ob) Gene Expression in Adipose Tissue in Mice and Altered Gene Expression in C57BL/6J ob/ob Mice," <i>The Endocrine Society, Programs and Abstracts</i> , 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.175 (ABSTRACT P1-249).
	C83	Olefsky, J.M., "Weighing in on the Lean Genes," <i>Journal of Clinical Investigations</i> , 95:2427-2428 (June, 1995).
✓	C84	Palmiter, R.D. et al., "Metallothionein-Human GH Fusion Genes Stimulate Growth of Mice," <i>Science</i> , 222:809-814 (November, 1983).

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## INFORMATION DISCLOSURE STATEMENT

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